Sept. 10, 1957

Dear Esther and Josh,

You probably want to know how the virus symposium got along, so I will try to give you one uninformed listener's view, namely, mine.

The first speaker, Andrewes, tried his hand at defining terms, which later became a sorepoint for all. "Latent" was to apply to a chronic and balanced infection while "masked" referred to a virus which is detected only by diverse means or with difficulty. "Inapparent" infection fits in somewhere, but I'm not sure just how (subclinical?). You might be interested to learn that since "clinical" refers to bed, "subclinical" means under the bed, to add to the terminology turmoil. Then he accounted for virus activation via other diseases, chilling, hormones, passage to susceptible hosts, etc. Next, hereditary transmission of "vegetative" virus, and possible function of incomplete virus in nature. The remainder of his talk concerned mechanisms by which viruses remain latent: e.g., mixed with antibodies or other inhibitors, too few in # to be detected, in vegetative phase, as provirus, too slow growing, etc.

Lwoff followed. He began with two new (?) terms, GMP (genetic material of phage) and phoron (unique site on bacterial chromosome where GMP attaches). He skimmed through the infection cycle and most likely hypotheses of GMP attachment in lysogenic cells. (By the way, he stressed using "bacterium" instead of "cell".) Next came superinfection of lysogenic bacteria by homologous phage, which penetrates but doesn't infect, being diluted in subsequent generations. Photoreactivation studies show immunity is lost by detachment of GMP. Then he mentioned virulent inducer mutants specific for a certain prophage, and showed that prophage modifies attachment 1, as a gene and 2, so that GMP cannot initiate phage development. "Dysgonia" followed -- I think this is a phenomenon whereby one phage can immunize a cell against a different phage which it would otherwise accept; but the immunity may be reversed by an unrelated mutation, as $S^S \rightarrow S^R$, or by physiological conditions. Then came induction emphasized as an initial disturbance in the bacterium, not in the phage (for both induced and spontaneous) -- organic peroxide mechanism. # of nonlysogenic to lysogenic conversions is constant but can be modified by chloromycetin, heat, etc, in early part of cycle -- immunity is established rapidly, as soon as attachment occurs. Next he explained how neither of 3 phages could lysogenize separately but any 2 together could, a copulation of sorts. He then explained that 98% lysogenization is achieved in some systems because of a 100 minute block of DNA^A, RNA^A, etc., syntheses in cells, leaving plenty of time for GMP to reach chromosome and produce immunity -- GMP behavior controlled by bacterium. Finally he mentioned defective lysogenics, with example of absence of endolysin to prevent lysis but cell still killed -- also absolute defectives (=latent infection, masked phage). Oh -- forgot -- he gave evidence for a ring chromosome, but I didn't catch it.

Beard ended the morning session with a lively exposé of masking and unmasking mechanisms. He stressed importance of the host in such activities as activation by provocative stimulation and least # of viruses needed for infectivity. In reference to latter requirement, he told how difficult it was to assay a virus producing warts (?) on rabbits (?) because so many millions were necessary to infect; but now there is a 10,000 fold increase in sensitivity of the assay by first painting the area to be infected with turpentine or methylcholanthrene (sp?). He described physiological latency as a result of the cell not being receptive, dormant infection as one capable of being induced, and occult infection as a commensalism situation.

Dulbecco started the afternoon session with postulating an affinity of the DNA's of host and virus in lysogenic-like relationships but not in virulent. He explained semi-temperate phages as those that allow the host bacterium to divide a few times before lysing -- these are highly UV resistant phages. He then devoted considerable time to a chart showing the 3 types of viruses, moderate, semimoderate, and virulent, and examples of each among plant, animal and bacterial viruses. Later in the afternoon,

another speaker -- perhaps Huebner -- suggested that "immoderate" was a better term than "virulent", and this change was generally accepted in discussions thereafter.

The next morning Puck talked about his current research, which was unfortunate for him in the sense that he couldn't answer obvious questions. He told that they can select single cell resistants in mammalian cells -- also single cell bursts. He defined a genome mutant as any genitically changed somatic cell! In his experiments, he used Newcastle's virus on HeLa cells in virus inactivating (+20% human serum) and virus stable media. H/MDV or H/M = Newcastle resistant He La cells. H/M doesn't adsorb virus, although high multiplicity -- more than 7 -- destroys them. By using a strain of multinucleate, giant cells which are good indicators -- very susceptible to Newcastle's -- he found that H/M cells are carriers. H/M cells plated on an X-rayed layer of giant cells form either plaques ~~of~~ or colonies depending on conditions. The same cells that are plaque formers ~~of~~ can also be colony formers. When H/M's are grown for several days in 1% antiserum and then transferred to virus stable medium, they cannot form ~~p~~ plaques but still remain resistant. After a few days in this standard medium, plaque forming ability returns. He postulates that the carried virus lies near the cell periphery where it can be reached by antiserum and that this virus-carrying state must be very stable to compete with antiserum. He likens the situation to lysogeny in that the virus is carried and able to be invoked, but different in that lysogenic cells are not affected by antiserum and the provirus is associated with the chromosome. (Newcastle's is an RNA virus as far as can be determined.) Perhaps the larger surface of giant cells provide ample sites ~~of~~ for such "peripheral" viruses. He hasn't yet followed virus release from single cells in this system. And he claims that the transferred cells are free of contaminating (adsorbed) antibody. Maybe! (The last word was my own claim.) Best of all, he uses our baby petri plates. Had some with him. I believe it was Puck who was excited about a recent report of antiserum against nucleic acids of animal viruses, but someone in discussion (Stanley) strongly questioned the methods of the group reporting this.

Bawden concentrated on King Edward potatoes, which carry a virus active against tobacco plants. Condemned plasmagene hypothesis -- is an exogenous infection. He said that tobacco mosaic virus can account for 70% of the "plant's" protein, and still the plant doesn't suffer much. Mentioned day/night and temperature effects upon virulent symptoms.

Philip, the insect man, read his paper so fast and furiously that I missed ~~practically~~ practically everything. He spoke of latency as a logical goal, preferred ~~symbiote~~ symbiote to symbiont; insects contain antibacterial substances but no antibodies; no true insect passes virus hereditarily. Claims host does as much adapting as virus.

Ackerman reported on polio grown on He La cells. He spoke of host cell variation in susceptibility: carrier He La's have darkly staining nuclei, reduced respiratory rate, polar processes, smaller cytoplasm; some is completely resistant to polio, and resistance is not specific (possibly because of less cytoplasm in "resistant" cells) -- resistance remains after disinfection. Next he spoke of phenotypic variation among viruses, as there is always a fraction which can't be neutralized by antibody; however, flourophenylalanine + antibody → complete inhibition. Trypsin + antibody washed cells clean.

Well, that's about all I thought worth telling you -- the others I either missed or didn't get anything ~~from~~ from.

Now for a non-academic, personal critique of the symposium, unsolicited though it may be. As a whole, it was worthwhile and satisfying. Of the speakers that I heard, only 3 -- Andrewes, Beard and Ackerman -- did not read their talks, which to me is a grievous fault. Beard and Ackerman --maybe Bawden, too -- were the genuinely human elements, especially Beard, who was rather outspoken and refreshing. I'm sure they were appreciated as perker-uppers. The discussions were not inspirational, centering mostly around terminology and running in semantic circles, although they brought out the problem most graphically. (The final panel settled upon some definitions which I won't attempt to relay.) The schedule went along smoothly, and the audience appeared attentive and interested. Wisconsin people remained conspicuously silent.

News on the home front is slim. Until a few days ago, lab has been rather quiet. Now things are more normal, with people back from vacations and otherwise. We have a new dishwasher, a Venezuelan who speaks not much English. The square petri plates haven't arrived yet. Alan got a new apartment. Iino seemed to enjoy his summer with Van Niel. Part of my family visited a few days in Madison, and then I drove to Schenectady with them and stayed there a week. I guess you know that Bob's operation was successful -- they stayed with us a while, and now Mari is back by herself, finishing her thesis -- her final exam is on the 27th. Monona Terrace is still up in the air. Milton fell into hot dishwater and nearly experminated himself. Ann's sister is visiting.

We now have 18 more L-form mutants, but all are mixed within each colony and some are downright grotesque. But more of that in the next letter, when I hope to have more information. Till then (which won't be so long in arriving) --

Yours,

Jacky

P.S. About the Mitchner book; none of the bookstores (including Paul's) had it, so I didn't do anything further. I can order it if you wish.

P.P.S. There are more pictures than the enclosed